## REMARKS

Previously, Claims 67-102 are pending. In the instant amendments, Claims 75, 83-91 and 99-102 have been canceled. Claims 67-74, 76-82 and 92-98 have been amended. After entry of the instant amendments, Claims 67-74, 76-82 and 92-98 will be pending and under consideration.

## I. THE AMENDMENTS TO THE SPECIFICATION

The "Table of Contents" at pages i-iv of the specification has been deleted to comply with 37 C.F.R. § 1.52(b).

The specification has been amended to include appropriate information regarding the deposit of microorganism pursuant to MPEP § 2411.05 and 37 C.F.R. § 1.809(d).

The specification has also been amended to include a proper priority benefit claim. Applicants submit herewith a Petition to Accept an Unintentionally Delayed Claim for Priority under 37 C.F.R. § 1.78. If the Petition is granted, Applicants respectfully request entry of the amendment to the specification.

Since these amendments do not include new matter, entry of the amendments to the specification is respectfully requested.

## II. THE AMENDMENTS TO THE CLAIMS

Claims 75, 83-91 and 99-102 have been canceled without prejudice to Applicants' right to pursue the subject matter of the canceled claims in one or more related application(s).

Claims 67, 76 and 92 have been amended to recite, in relevant part, "an isolated or recombinant antibody." Support for amended Claims 67, 76 and 92 can be found, in the specification, for example, at page 44, lines 9-24, page 56, line 3, to page 58, line 14, page 88, lines 2-10, and page 88, line 33, to page 89, line 1.

Claim 76 has been further amended. Support for the amendment to Claim 76 can be found, in the specification, for example, at page 10, lines 21-25, page 56, line 3, to page 58, line 14, and page 84, lines 15-22.

As the amendments do not introduce any new matter and are fully supported by the specification of the present application, entry and consideration thereof is respectfully requested.

## III. PRIORITY

The priority claim to the benefit of the filing date of the parent application, U.S. Application Serial No. 08/386,844 ("the '844 application"), now Pat. No. 6,156,500, has been denied.

The Patent Office first alleges that Applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 120. Applicants submit that Applicants did not identify all applications and their relationship in their priority claim in the application as originally filed. The error was unintentional. Applicants submit herewith a Petition to Accept an Unintentionally Delayed Claim for Priority under 37 C.F.R. § 1.78 ("the Petition"). Applicants' proper benefit claim should read as follows: "this is a continuation of Application Serial No. 09/176,330 ("the '330 application"), filed October 22, 1998, now abandoned, which is a divisional application of Application Serial No. 08/485,573 ("the '573 application"), filed June 7, 1995, now Pat. No. 5,968,770, which is a continuation-in-part of Application Serial No. 08/386,844, filed on February 10, 1995, now Pat. No. 6,156,500." Upon acceptance of the Petition, Applicants respectfully request that the specification be amended, as discussed above.

The Patent Office also alleges that the priority claim to the filing date of the '844 application is not justified, because the claimed invention recites antibodies specific for rchd523 gene product and the '844 application did not disclose any coding sequence of rchd523. The Patent Office acknowledges the claim for domestic priority under 35 U.S.C. § 120 to the '330 application, which discloses the full length sequence of rchd523, once Applicants comply with 35 U.S.C. § 120. Applicants respectfully submit that the '573 application, *i.e.*, the parent application of the '330 application, also disclosed the full length sequence of rchd523 at columns 75-78 (DNA sequence) and columns 95-98 (amino acid sequence) of the issued patent. Thus, Applicants submit that the claims of the instant application is entitled to the benefit of the filing date of the '573 application. Upon

acceptance of the Petition, Applicants respectfully request the priority claim to the benefit of the filing date of U.S. Application Serial No. 08/485,573, filed June 7, 1995, be entered.

## IV. THE REJECTION OF CLAIMS 67-69, 76-78 AND 92-94 UNDER 35 U.S.C. § 101

Claims 67-69, 76-78 and 92-94 stand rejected, under 35 U.S.C. § 101, because the claimed invention is allegedly directed to non-statutory subject matter. Specifically, the basis for this rejection appears to be that the claims might read on a product of nature in its native milieu.

Claims 67, 76 and 92 have been amended to recite, in relevant part, "an isolated or recombinant antibody." As such, the claims as amended can no longer read on naturally occurring antibodies in their native milieu. Applicants submit that the rejection of Claims 67, 76 and 92, and claims that depend from these claims is obviated in view of these amendments. Accordingly, Applicants respectfully request that the rejection of Claims 67-69, 76-78 and 92-94 under 35 U.S.C. § 101 be withdrawn.

## V. THE REJECTION OF CLAIMS 75-91 AND 99 UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 75-91 and 99 stand rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

First, the Patent Office alleges that in Claims 75, 83, 91 and 99, the term "another therapeutic antibody" is unclear. Although Applicants do not agree and in no way acquiesce to this rejection, to solely expedite the prosecution, Claims 75, 83, 91 and 99 have been canceled. Accordingly, Applicants respectfully request the rejection of Claims 75, 83, 91 and 99 under 35 U.S.C. § 112, second paragraph, be withdrawn.

Second, the Patent Office alleges that in Claims 76 and 84, the term of "analogs thereof" of the rchd523 protein is unclear, because it is unclear how close to the original rchd523 sequence an analog might be. Claim 76 has been amended to delete the term "analogs thereof." Claim 84 has been canceled without prejudice. Applicants submit that the rejection of these claims is moot in view of these cancellation of and amendments to these

claims . Accordingly, Applicants respectfully request that the rejection of Claims 76 and 84 under 35 U.S.C. § 112, second paragraph, be withdrawn.

In view of the foregoing, Applicants respectfully request the rejection of Claims 75-91 and 99 under 35 U.S.C. § 112, second paragraph be withdrawn.

## VI. THE REJECTION OF CLAIMS 67-99 UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 76-91 and 99 stand rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of written description. Claims 67-99 stand rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Applicants respectfully transverse the rejections.

### A. The rejection of Claims 76-91 and 99 for lack of written description should be withdrawn

Claims 76-91 and 99 stand rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of written description. Specifically, the Patent Office contends that the "analogs of rchd523" and "another therapeutic antibody" are not fully supported by the specification. Applicants respectfully disagree and do not acquiesce to this rejection. Nevertheless, to expedite prosecution, Applicants have amended Claim 76 and have canceled Claims 83-91 and 99 without prejudice. Applicants submit that the rejection of these claims is moot in view of the cancellation of and amendments to these claims. Accordingly, Applicants respectfully request that the withdrawal of this rejection of Claims 76-91 and 99 under 35 U.S.C. § 112, first paragraph.

### B. The rejection of Claims 67-99 for lack of enablement should be withdrawn

Claims 67-99 stand rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. In particular , it is alleged that the claims are not enabled because: (1) an antibody "immunospecifically" binds to rchd523 is taken to mean an antibody that binds to rchd523 only; and (2) the specification fails to provide guidance and working examples on how to produce the antibody, which can distinguish rchd523 and protein CMKLR2, which differs from rchd523 by one residue and was disclosed in Owman *et al.*, Biochem. Biophys. Res. Comm. Vol. 228:285-292 ("Owman *et al.*"). For the reasons set forth below, Applicants respectfully disagree.

### 1. Legal standard

Applicants again directs the Patent Office's attention to the legal principles governing enablement requirement. Before any analysis of enablement can occur, it is necessary for the Patent Office to construe the claims. *Manual of Patent Examining Procedure* ("MPEP") § 2164.04. During patent examination, the pending claims must be given their broadest reasonable interpretation consistent with the specification. *In re American Academy of Science Tech Center*, 367 F.3d 1359, 1364, (Fed. Cir. 2004); MPEP § 2111. The broadest reasonable interpretation must also be consistent with the interpretation that those skilled in the art would reach. *In re Cortright*, 165 F.3d 1253, 1359 (Fed. Cir. 1999).

The legal standard for enablement under 35 U.S.C. § 112, first paragraph, requires that the specification teach those skill in the art to make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." *United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988). The Patent Office bears the initial burden of establishing a reasonable basis for questioning the enablement of the claimed invention. *In re Wright,* 999 F.2d 1557, 1562 (Fed. Cir. 1993); MPEP § 2164.04. Furthermore, "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied." MPEP § 2164.01(b), citing *In re Fisher*, 427 F.2d 833 (CCPA 1970).

### 2. The rejection of Claims 67-99 for lack of enablement should be withdrawn

Here, a *prima facie* case of lack of enablement has not been established. First, Applicants respectfully disagree with the Patent Office's interpretation of "immunospecifically." The Patent Office interprets "immunospecifically bind" as absolute specificity, requiring a complete inability to bind to any other target molecule. Applicants submit that "immunospecifically" is not so narrowly understood by one skilled in the art. As will be understood by one skilled in the art, "immunospecifically bind" means that an immunoglobulin molecule, or an antibody, that specifically binds an antigen and does not non-specifically bind to other polypeptides. An antibody that specifically binds to an antigen may be cross-reactive with other antigens. *See, e.g.*, Paul *et al.*, Fundamental Immunology, (Raven Press, New York, 2d ed. 1989) at page 332-336 (attached as Exhibit A). Particularly,

since the same epitopes might be present on different antigens, antibodies that specifically bind antigen A may bind antigen B, if antigen A and antigen B share one or more epitopes. *See, e.g.*, Golub *et al.*, Immunology A Synthesis, (Sinauer Associates Inc., 2d ed. 1991) at page 27 (attached as Exhibit B). Further, as will be understood by one skilled in the art, an antibody that immunospecifically binds to rchd523 gene product as recited by the instant claims can specifically bind to rchd523 gene product, as determined using experimental techniques, such as radioimmunoassays (RIA) and enzyme-linked immunosorbent assays (ELISAs).

The PTO alleges that the specification fails to provide guidance and working examples on how to produce the antibody, which can distinguish rchd523 and protein CMKLR2, which differs from rchd523 by one residue and was disclosed in Owman *et al.*, published September 30, 1996. As discussed above, the term "immunospecifically" allows for cross-reactivity with other polypeptides that share epitopes with rchd523 polypeptides. In addition, Applicants submit herewith a Petition to Accept an Unintentionally Delayed Claim for Priority under 37 C.F.R. § 1.78, requesting that a priority claim for the benefit of the filing date of U.S. Application Serial No. 08/485,573 be entered. Upon grant of the petition and request, the priority date of the instant application will be June 7, 1995, which is prior to the publication date of Owman *et al.*

Moreover, the specification of the present application coupled with information known as of the effective date of the present application provides sufficient guidance to enable one of skilled in the art to make and use the claimed antibody without undue experimentation. Rchd523 gene product, the antigen of the claimed antibody, is described in detail in the specification. For example, the specification discloses the nucleic acid and amino acid sequence of rchd523. *See* Specification, Figure 28A and 28B. The specification teaches that rchd523 gene product is a G-protein coupled receptor. *See* Specification, page 129, lines 29-34; page 132, lines 28-33. The specification also teaches that rchd523 gene product is up-regulated upon shear stress in endothelial cells. *See* Specification, Figure 26 and 27; page 102, lines 22-31; page 129, lines 21-23.

In addition, methods for producing antibodies that immunospecifically bind to rchd523 gene product are described in the specification of the present application and were well known as of the effective filing date of the present application. *See* Specification

page 56, line 1 to page 58, line 14; page 88, lines 1-10; Chapter 14 of Harlow *et al.*, 1988, Antibodies A Laboratory Manual, Cold Spring Harbor, New York. An antibody that binds to rchd523 gene product can be identified, for example, by immunoassays, BIAcore, or other techniques known to those of skill in the art.

Furthermore, the specification teaches the use of the claimed antibody, for example, in the diagnosis of cardiovascular disease by *in vivo* tissue image techniques. *See* Specification page 102, line 32, to page 103, line 29. Thus, contrary to the Patent Office's contention, the teachings provided in the specification, coupled with the state of the art with respect to antibodies would enable one skilled in the art to make and use the claimed antibody without undue experimentation.

Accordingly, Applicants respectfully request the rejection of Claims 67-99, under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement, be withdrawn.

### C. The rejection of Claims 92-99 based on recitation of deposited material should be withdrawn

Claims 92-99 stand rejected because the Patent Office asserts that the claims make reference to deposited materials but the specification does not make appropriate reference to availability of the deposited material upon issuance of a patent from the instant application. The Patent Office also contends that an affidavit or declaration by Applicants, or statement by an attorney of record is required to assure that the deposited material recited in Claims 92-99 will be irrevocably and without restriction released to the public upon the issuance of a patent.

The specification has been amended to fully identify the deposit accession number, name and address of the depository, and description of the deposited material. In addition, Applicants respectfully direct the Patent Office's attention to the attached Statement by the attorneys for the Applicants which attests to the deposit of microorganisms, in compliance with the criteria set forth in 37 C.F.R. §§ 1.801-1.809 regarding the availability and permanency of deposits. Thus, the amendment to the specification and the Statement obviate the rejection based on the availability of the deposited material recited in Claims 92-99.

Accordingly, Applicants respectfully request that the rejection of Claims 67-99 under 35 U.S.C. § 112, first paragraph be withdrawn.

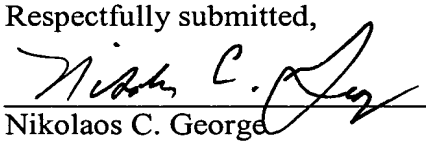
## CONCLUSION

In light of the above remarks, Applicants respectfully request that the Examiner reconsider this application with a view towards allowance. Applicants submit that Claims 67-74, 76-82 and 92-98 satisfy all of the criteria for patentability and are in condition for allowance. The Examiner is invited to call the undersigned attorney at 650-739-3939 if a telephone call could help resolve any remaining items.

No fees, other than the fee for petition under 37 C.F.R. §1.78 and for extension of time under 37 C.F.R. § 1.136(a), are believed due in connection with this response. However, pursuant to 37 C.F.R. §1.136 (a)(3), the Commissioner is authorized to charge all required fees, fees under 37 C.F.R. §1.17 and all required extension of time fees, or credit any overpayment, to Jones Day Deposit Account No. 50-3013 (709181-999242).

Respectfully submitted,

Date: **April 5, 2005**



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